IV. AMENDMENTS TO THE DRAWINGS

- *THE DRAWINGS OF THE PATENT IS HEREBY AMENDED AS SET FORTH BELOW:*

  - **There are no amendments to the drawings.**

V. REMARKS/ARGUMENTS

- *STATUS OF CLAIMS*

With this "RESPONSE TO OFFICE ACTION," claims 41 through 49, claims 51 through 61, and claims 63 through 74, are pending. Claims 1 through 40, 50 and 62 are cancelled without prejudice.

- *AMENDMENTS TO CLAIMS*

The claims have been amended as shown in section III. No new matter has been added.

- OBJECTIONS

OBJECTIONS TO CLAIMS

- *Examiner's Stance*

The Examiner has objected to claim 49 and required appropriate correction with specified text. Examiner has objected to claims 43, 46, 52, 60, 61 and 64 on the basis that they are dependent on a rejected base claim. These claims would be allowable if rewritten in independent form.

- *Applicants' Response*

The Applicant has amended claims 49 as required by Examiner.

With respect to claims 43, 46, 52, 60, 61, and 64, while Applicant appreciates Examiner's conditional allowance of subject claims, Applicant is traversing rejections of the respective base claims in the following sections. Applicant therefore believes that the grounds for the objections to claims 43, 46, 52, 60, and 61 are moot.

REJECTIONS UNDER 35 U.S.C. §112

- *Examiner's Stance*

The Examiner rejected claims 50, 58, and 59 as being indefinite under *U.S.C. §112,* second paragraph.

- *Applicants' Response*

The Applicant has cancelled claim 50 thereby making the rejection moot. The Applicant has amended claims 58 and 59 to comply with *U.S.C. §112,* second paragraph, as required by the Examiner.

REJECTIONS UNDER 35 U.S.C. §102

- *Examiner's Stance*

The Examiner has rejected claims 55, 57 and 59 under *35 U.S.C. §102,* as being anticipated by Bassi, et al.

- *Applicants' Response*

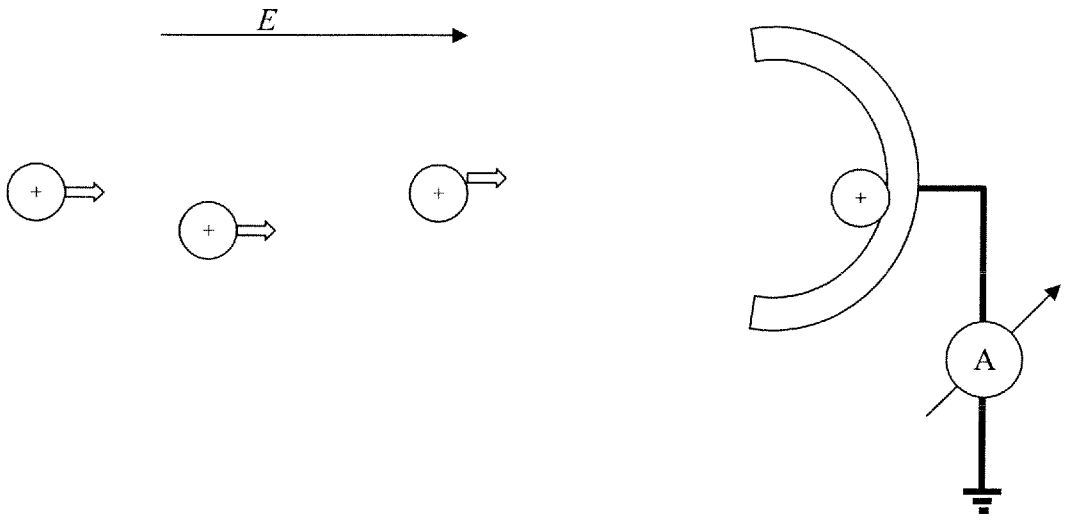
Before addressing the specific rejections, the Applicant would like to offer some comments about the types of prior art for detecting ions.

In general, there are two types of prior ion detecting techniques:

(A) Faraday Cup; and
(B) Electron multiplier.

(A) Faraday Cup

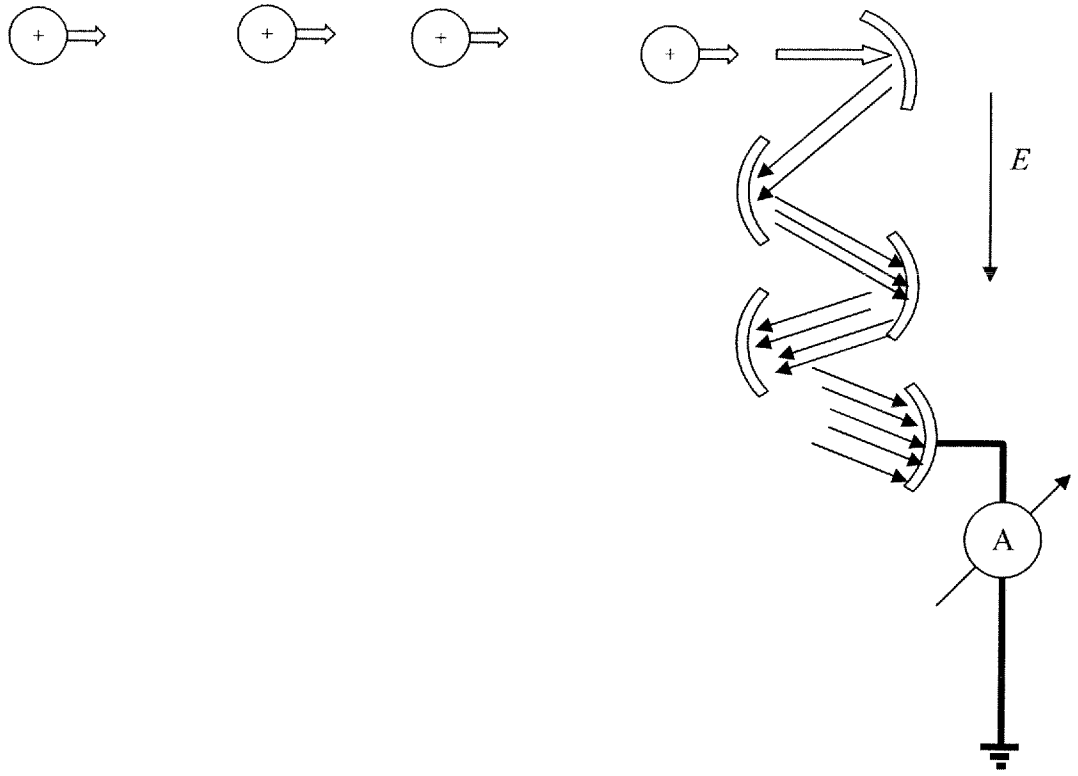
The concept is very simple: ions in a gas can be moved against a conductive object using an electric field. The resulting electric current through the object can be measured.



The low detection limit is between about 10^{12} to 10^{15} ions/cm^3 i.e. that is equivalent to a level of detection of parts per million (ppm) to parts per billion (ppb); this results from thermal noise in the electric circuit. It is not possible to detect individual ions with this method.

(B) <u>Electron multiplier</u>

An electron multiplier requires a vacuum. Individual ions impact an electrode and cause secondary emission of between one and several electrons. These electrons are accelerated by an electric field to another electrode to repeat the first process. In this way it is possible to cause an avalanche of electrons over several electrodes. The resulting current (or voltage) can be detected at the final electrode.



Once part of a sample reaches the vacuum in the electron multiplier the low detection limit of such an apparatus is one ion. This translates to a low detection limit in the sample (e.g. of air) of between about 10^{12} to 10^{15} ions/cm^3 i.e. equivalent to ppm to ppb level. The poor sensitivity based using an air sample is due to losses of ions in the interface between the air pressure environment and the vacuum necessary to operate the electron multiplier.

With respect to the rejection of claims 55, Bassi, et al. do not disclose an apparatus for counting individual ions in a gaseous sample that does not use a vacuum. In Fig. 3 of Bassi various pumps are shown connected to the reaction chamber (referred to as "ultra-high vacuum chamber" in the text); thus Bassi requires a vacuum to detect individual ions. Therefore Bassi does not disclose an apparatus of the type required by claim 57 (previous claim 55).

Furthermore in the reaction chamber of Bassi primary ions are used to generate product ions from a sample gas. The mixing chamber of claim 57 is not required to do this. In particular, the mixing chamber allows the ions in a sample gas to collide with particles (each very much larger than an ion), whereby the particles become charged in any of the ways described in the specification. No secondary or product ions are produced by the mixing chamber of claim 57.

Finally, Bassi does not disclose a separation chamber having the various inlets and outlets claimed for passing two streams of gas through the mixing chamber; nor does Bassi disclose an electric field generating means capable of moving charged particles, each of which has a mass greater than one ion and is of a size dectectable and countable by a single particle counting apparatus. As the Examiner notes, Bassi discloses a mass spectrometer suitable for counting ions *per se*. As such it uses technology of the type described at (B) above and is therefore not suitable for counting individual ions without using a vacuum.

With respect to the rejection of claim 57, Bassi does not disclose electrodes operatively configured for moving charged particles of the size and mass defined in claim 57.

With respect to the rejection of claim 59, Bassi does not disclose a ionisation chamber for ionising molecules of interest attached to an inlet of the mixing chamber. In Bassi, ionisation of the molecules of interest takes place within the reaction chamber or scattering cell (which the Examiner has equated with the mixing chamber of claim 57).

REJECTIONS UNDER 35 U.S.C. §103

- *Examiner's Stance*

The Examiner has rejected claims 41, 42, 44, 49, 50, 53, and 54 under *35 U.S.C. §103* as being obvious over Eiceman in view of Zhang, et al.

- *Applicants' Response*

Applicant notes that the basis for factual inquires, with respect to findings of obviousness under 35 U.S.C. 103, are set forth in accordance with *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966), the primary indicia being summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

Further, the Applicant calls the Examiner's attention to MPEP 2143.03 which states that to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. On that basis alone, the cited prior art fails to provide a basis for a finding of obviousness.

Specifically with regard to claim 41, Eiceman does not disclose the step of colliding ions with uncharged particles of a size countable by a single particle counting method. In particular, in the section "Ion formation" of Eiceman a molecular analyte M (corresponding to "uncharged particles" in claim 41 according to Examiner) reacts with reactant ions to form protonated monomers. Prior to the reaction, the molecules of the analyte (such as Dichloromethane or other such molecules) are not countable by a single particle counting method as required by claim 41.

To detect (as distinct from count) ions Eiceman teaches use of an electrometer using the type of technology described under (A) above. As such individual ions are not countable due to electrical noise as described above. This is a major limitation of technology (A) that makes it impossible to count individual ions.

The Examiner asserts that the skilled person would use the teaching of Zhang to remedy the deficiencies of Eiceman. However, claim 41 now requires the method to be performed without using a vacuum, whereas Zhang relies on a vacuum (see mechnical pump, diffusion pump and turbo pump in Fig. 1 on page 4003). The critical factor in Zhang is the combination of a vacuum pump and mesh cylinder in the ion guide which allows the neutral molecules to be

separated from the ions. This is in direct contrast to claim 41 in which the method operates without using a vacuum.

Furthermore Zhang relies on the electron multiplier technology of type (B) described above. In the methodology of Zhang most of the ions are lost to the ion guide, diffusion pump and quadrupole filter such that only a very small number (perhaps one or two) reach the multiplier. Due to such high losses, a very large number of ions must be present in the flow tube of Zhang if any are to reach the multiplier. Accordingly the low detection limit of a combination of Eiceman and Zhang is not improved beyond the ppm to ppb level.

The present invention is based on the insight that particles of a size large enough to be counted individually can be employed to count the number of individual ions in a gaseous sample. Mixing of the ions of interest with such particles causes a number of those particles to become charged by only one ion each. Following that, separation of the charged particles from the uncharged particles allows the number of charged particles to be counted using more accurate technology than attempting to count ions using the technology of the types (A) and (B) e.g. Eiceman and Zhang.

The invention does not rely on measurement of voltage or electric current to detect ions. In particular embodiments of the invention, particles of a size 10^9 times greater in size than the ions of interest are used to count the ions indirectly. For example the ions may be of about 0.3nm in diameter, whereas the particles may be 0.3μm in diameter. In some embodiments the particles are so large that they can be seen with the naked eye.

This technique radically improves the low detection limit (from 10^{15} ions/cm^3 down to 10^2 ions/cm^3 in the sample gas). The prior does not even hint that such an improvement might be possible.

With respect to claim 42, Zhang does not teach combining and mixing two separate flows of gas. In Zhang only one inlet is taught through which a carrier gas is input (see Fig. 1 and page 4002 col. 2 lines 5-9).

With respect to claim 44, Zhang does not teach particles of greater than or equal to 0.3μm diameter. "Neutral molecules" are taught in Zhang (see page 4003 second paragraph).

With respect to claim 45, Sinha teaches that aerosol particles can be examined by vaporizing and ionizing them (see Sinha col. 2 lines 31-32) and then analysing the ions using a mass spectrometer (requiring a vacuum). No teaching is presented by Sinha that aerosol particles can be used as a tool to count the numbers ions (already generated elsewhere) in a gas sample as per the methodology of the invention.

Claim 45 in combination with claim 41 requires aerosol particles to be used to facilitate counting of ions in a sample gas, rather the to use the aerosol particles as a source of ions as per the teaching of the combination of Eiceman and Sinha.

With respect to claim 47, for similar reasons as per claim 45, it is submitted that the particles being a hydrosol or emulsion is not obvious in view of the combination of Eiceman and Sinha.

With respect to claim 48, Sinha does not teach that the aerosol particles should be counted by any of the means mentioned in this claim. The purpose of the two lasers in Sinha is simply to detect and to vaporise particles when detected. It would serve no purpose for Sinha to teach that aerosol particles should be counted since ions are only present in Sinha's method after the aerosol particles have been vaporised.`

With respect to claim 49, the amended claim now requires that pre-selection of ions by an ion mobility selection unit take place before mixing in the mixing chamber. No such teaching is made in Eiceman or Zhang.

Claim 50 has been canceled without prejudice.

With respect to claim 51, the combination of Eiceman, Zhang and Sinha does not teach the steps of heating or evaporating a liquid or solid to form a gas sample and performing the steps of claim 41 on the gas sample.

With respect to claim 53, neither Eiceman nor Zhang teach using a differential mobility analyser to separate charged particles from uncharged particles, the particles being of the size required by claim 41.

With respect to claim 54, neither Eiceman nor Zhang teach the step of impinging charged particles of a size required by claim 41 onto a detecting and numerical measuring means so as to indicate the charge carried thereby.

With respect to claim 56, Fig. 1 of Eiceman discloses a Faraday plate detector. This is of detection type (A) described above in which it is explained that detection of individual particles is not possible due to thermal noise in the circuit. Therefore claim 56 is not obvious in view of the combination of Bassi and Eiceman.

With respect to claim 58, Bassi makes no teaching of pre-selecting ions of a pre-determined mobility before supplying them to a mixing chamber. Rather Bassi teaches the use of a 90° magnetic mass spectrometer to select that primary ions that are used to generate the ions of interest. Bassi provides no teaching of using an ion mobility selection unit to select ions of interest.

Claim 62 is canceled without prejudice.

With respect to claim 63, Bassi and Sinha each teach a different way of generating ions for analysis by a mass spectrometer: Bassi teaches reacting primary ions with molecules of a gas, whereas Sinha teaches vaporising and ionising aerosol particles. Since each technique works at size scales that are many orders of magnitude apart, one of ordinary skill would not combine the two teachings in the way suggested by the Examiner.

In conclusion, the present invention is based on the insight that particles of a very large size (e.g. on the micrometer scale) can be used to count individual ions (on the nanometer scale) in a gas sample. The realisation is that by mixing the sample of gas with such particles, one particle can become charged by only one ion; once charged other ions are repelled from that particle. The charged particles can then be separated from the uncharged particles using an electric field. Due to their large size the charged particles are countable by a single particle counting method to give very accurate results. The combination of each particle being chargeable by only one ion, separating the charged particles from the uncharged particles, and counting the charged particles gives unexpectedly accurate results and achieves an improvement of the low level detection limit in the gas sample by a factor of 10^{10} to 10^{13}.

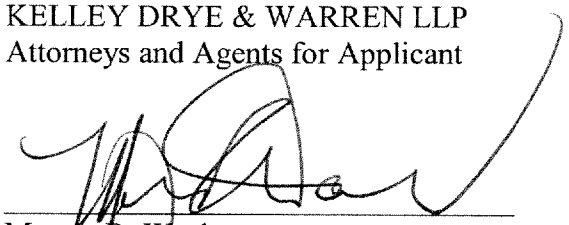
The method of the invention takes a direction entirely contrary to the prior art, which relies on the established techniques of types (A) and (B) above. The present invention places no such reliance on those techniques.

CONCLUSION TO REMARKS

Applicant asserts that this response is fully responsive to the Examiner's Office Action dated August 24,, 2007. In view of the above, it is respectfully submitted that the subject matter of the pending claims is patentable over the references cited. Applicant respectfully seeks early allowance of the pending claims.

December 17, 2007

Respectfully Submitted,
KELLEY DRYE & WARREN LLP
Attorneys and Agents for Applicant



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VI. APPENDIX

- *No appendix is intended to be attached*